

R E M A R K S

New Claims

Original claims 1 to 10 were canceled hereinabove, and new claims 11 to 21 were added.

The terminology of "pharmaceutically acceptable salt" recited in the new claims is supported in the specification on page 27, lines 3 to 15.

New claim 11 contains features of original claims 1 to 4. The recitation of a "cycloalkyl group" as a substituent of the substituted alkoxy group in new claim 11 is supported in the specification by Compound 5-73 on page 192. The remainder of the terminology in new claim 11 involving the "substituted alkoxy group" is supported in the specification on page 17, lines 15 to 23. The definition of the substituted alkylamino group in new claim 11 is supported on page 21, lines 12 to 20.

New claim 12 includes features of original claim 5.

New claim 13 includes features of original claim 5.

The benzylamino group recited in new claims 12 and 13 is supported by Compound 5-6 on page 165 of the specification.

New claims 14, 16 and 18 include the features of original claim 6.

New claims 15, 17 and 19 are supported in the specification on page 33, lines 3 to 18.

New claim 20 includes the features of original claim 7.

New claim 21 includes features of original claim 8.

#### Abstract

The Abstract as originally filed was replaced with the ABSTRACT OF THE DISCLOSURE appended hereto.

#### Rejections Under 35 USC 112, First Paragraph

1. Claims 9 and 10 were rejected under 35 USC 112, first paragraph, based on lack of enablement for the reasons set forth on pages 2 to 6 of the Office Action.

Claims 9 and 10 were canceled hereinabove.

2. Claims 1 to 10 were rejected under 35 USC 112, first paragraph, based on lack of enablement for the reasons set forth on pages 6 to 8 of the Office Action.

This rejection was on the ground that the specification is enabling for a "pharmaceutical salt" of formula (I) (see page 27, lines 3 to 15 of the specification), but is not enabled for a process for preparing all salt forms of formula (I).

Following the Examiner's suggestion, the present claims recite a "pharmaceutically acceptable salt."

Withdrawal of the 35 USC 112, first paragraph rejection is therefore respectfully requested.

#### Claim Objections

Claims 5, 6, 8, 9 and 10 were objected to under 37 CFR 1.75(c) as being in improper form for the reasons set forth on page 14 of the Office Action.

The present claims do not include any improper multiple dependent claims.

As noted above, claims 9 and 10 were canceled.

It is respectfully submitted that the new claims presented hereinabove are free of the reasons for the claim objections set forth in the Office Action.

#### Obviousness Rejection Under 35 USC 103

Claims 1 to 10 were rejected under 35 USC 103 as being anticipated [sic] by Reich et al. (USP 6,555,539) for the reasons set forth on pages 8 to 14 of the Office Action.

It was admitted on page 11 of the Office Action that the difference between USP 6,555,539 to Reich et al. and the instant claims is the R<sup>2</sup> variable of USP 6,555,539. It was stated in the Office Action that the R<sup>2</sup> variable of the instant application is always a phenyl or pyridine moiety substituted with -CH<sub>2</sub>NH<sub>2</sub>, whereas USP 6,555,539 teaches phenyl and pyridyl species, for example, that are substituted with -CH<sub>2</sub>-NH(alkyl) or -CH<sub>2</sub>-NH(aryl) or -CH<sub>2</sub>OH.

The position was apparently taken in the outstanding Office Action that since the compounds described in Reich et al. have a similar chemical structure as the presently claimed compounds, a person of ordinary skill in the art could conceive that the compounds of the presently claimed invention would exhibit the pharmacological actions disclosed in Reich et al. (medical use: inhibitory action of CDK4/D, CDK2/A, CHK1, VEGF, LCK, FGF, FAK and HCT116), and that the presently claimed invention is therefore obvious from Reich et al.

However, the chemical structure of the compounds of the presently claimed invention differ substantially from the chemical structure of the compounds of Reich et al. Furthermore, the compounds of the presently claimed invention greatly differ from the compounds of Reich et al. in their pharmacological

action (medical use). The positions set forth in the two preceding sentences are evidenced by the following points.

Firstly, the substituent  $R^3$  of the compounds of the presently claimed invention is a group shown in the following Fig. 1, i.e., a hydrogen atom, an alkyl group substituted with at least one group selected from the group consisting of a hydroxyl group and a hydroxyimino group, an unsubstituted alkenyl group, a carboxyl group or an ester or an amide thereof, an amino group, or a cyano group.

In contrast to the presently claimed invention, the  $R_1$  substituent (corresponding to the  $R^3$  substituent of the compounds of the presently claimed invention) of the compounds disclosed in the Examples of Reich et al. is a group shown in the following Fig. 2, i.e., a benzene ring, a pyrrole ring, a substituted or unsubstituted imidazole ring, a substituted or unsubstituted benzimidazole ring, or a substituent having an aromatic ring selected from a styryl and a pyrrolyliminomethyl as a constituent. All of the  $R_1$  groups of the compounds of Reich et al., which are especially pointed out on pages 10 to 13 of the Office Action that allegedly have a chemical structure close to the compounds of the presently claimed invention, are substituted or unsubstituted benzimidazole rings. That is, the compounds of

the presently claimed invention substantially differ from those of Reich et al., since the  $R^3$  substituent of the compounds of the presently claimed invention (corresponding to the  $R_1$  substituent of Reich et al.) are not an aromatic ring, and particularly are not a substituted or unsubstituted benzimidazole ring, whereas the compounds of Reich et al. that are exemplified in the Office Action have such a substituent as an indispensable constituent.

Fig. 1

Compound of the Present Invention

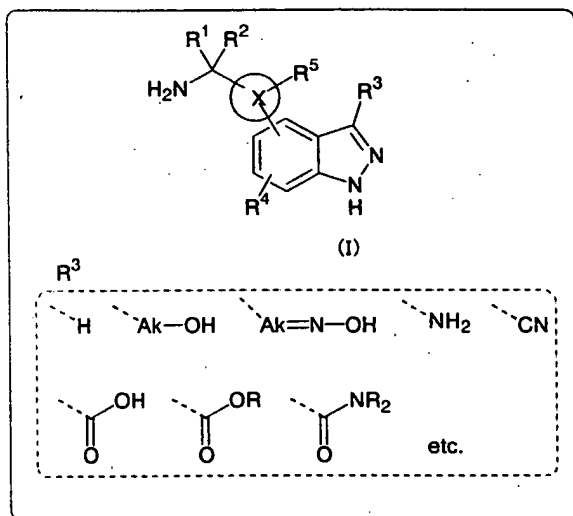
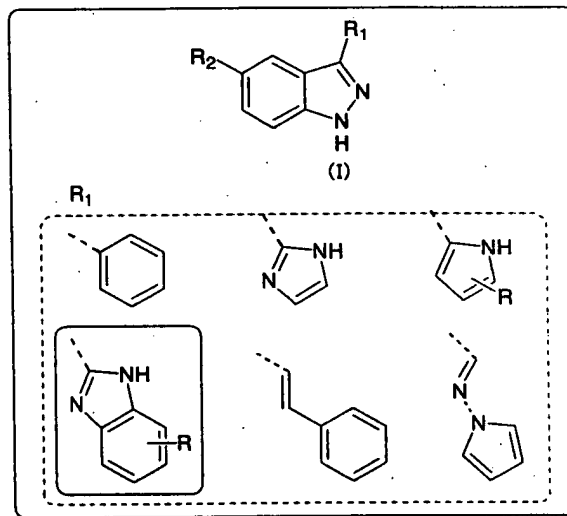


Fig. 2

Compound of the Reference



In view of the above, it is respectfully submitted that the compounds of the presently claimed invention greatly differ from that of Reich et al. in the chemical structure of the main skeleton with respect to the  $R^3$  substituent, (corresponding to  $R_1$  substituent of Reich et al.). Furthermore, to provide the pharmacological actions of the compounds of Reich et al., a

substituent having an aromatic ring, such as a substituted or unsubstituted benzimidazole ring, is required as a constituent.

Secondly, the presently claimed compounds substantially differ from the compounds of Reich et al. with respect to the pharmacological action afforded by the respective compounds. The pharmacological action of the compounds of the presently claimed invention is a Rho kinase inhibitory action and/or an intraocular pressure reducing action, whereas that of Reich et al. is an inhibitory action of CDK4/D, CDK2/A, CHK1, VEGF, LCK, FGF, FAK, and HCT116, an inhibitory action of cell proliferation, and other actions.

Thirdly, Reich et al. do not teach or suggest that their compounds have a Rho kinase inhibitory action and/or an intraocular pressure reducing action that the compounds of the presently claimed invention possess.

In summary, from the following four points, Reich et al. cannot be said to have any teaching, suggestion or motivation to lead one of ordinary skill in the art to arrive at the presently claimed invention:

- (1) The chemical structure of the compounds of the presently claimed invention greatly differ from that of Reich et al.
- (2) The pharmacological action of the compounds of Reich et al. are submitted to require an aromatic ring such as a substituted or unsubstituted benzimidazole ring as a substituent.
- (3) The pharmacological actions of the compounds of the presently claimed invention and Reich et al. are substantially different from each other.

(4) Reich et al. do not describe or suggest that their compounds have a Rho kinase inhibitory action and/or an intraocular pressure reducing action that the compounds of the presently claimed invention possess.

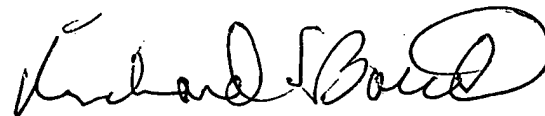
Withdrawal of the 35 USC 103 rejection is thus respectfully requested.

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,

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Enc.: PETITION FOR EXTENSION OF TIME